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## Surgical management and hypermetabolic modulation of pediatric burns

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*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2002

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Barret Nerín, J. P. (2002). *Surgical management and hypermetabolic modulation of pediatric burns*. s.n.

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# **Chapter 1**

## **GENERAL INTRODUCTION AND SCOPE OF THE THESIS**

The skin is the largest organ in the body, comprising 15% of body weight, and covering approximately 1,7 m<sup>2</sup> in the average adult. The function of the skin is complex: it warms, it senses, and it protects. Of its two layers, only the epidermis is capable of true regeneration. When the skin is seriously damaged, this external barrier is violated and the internal milieu is altered. A burn injury implies damage or destruction of skin and/or its contents by thermal, chemical, electrical, or radiation energies or combinations thereof. Thermal injuries are by far the most common and frequently present with concomitant inhalation injuries. In general, when destruction of living tissue far exceeds the capacity of regeneration, a full thickness injury develops with loss of the skin barrier. Necrotic cells and denaturalized proteins initiate a local and systemic response that, in extensive cases, starts a cascade of events that provokes a multiple organ dysfunction syndrome and eventually the death of the patient.

Severe burn injury may represent the most extreme stress along the spectrum of traumatic injuries. Burn injury, unlike other traumas, can be quantified as to the exact percentage of the body surface injured and can be viewed as a paradigm of injury from which many basic lessons can be learned about critical illness. Tissue injury after thermal trauma results from several factors. Most tissue is lost from heat coagulation of the proteins within the tissue. The final tissue loss, however, is progressive and results from release of local mediators, changes in blood flow, tissue edema, and infection. The fluid loss into the wound and release of cytokines into the systemic circulation result in a characteristic systemic response to thermal injury. In general, the initial period after burn injury is hypodynamic. Hypovolemia is the immediate consequence of fluid loss, resulting in decreased perfusion and oxygen delivery. During the subsequent hours to days the hemodynamic response becomes hyperdynamic. This period is characterized by marked increases in cardiac output, low systemic vascular resistance, and a pathologic inability to respond to hypovolemia with vasoconstriction.

The cytokine cascade causes a marked increase in metabolic rate with a profound increase in resting energy expenditure, resulting in glycolysis and gluconeogenesis through the breakdown of muscle. Patients who have sustained serious burn injuries demonstrate also a marked decrease in their immune status and ability to resist infection. Immunosuppression from massive tissue injury, necrotic tissue, and bacterial translocation, make infection one of the major cause of death in patients who survive beyond the initial resuscitation period, second in incidence to inhalation injury and acute respiratory distress syndrome.

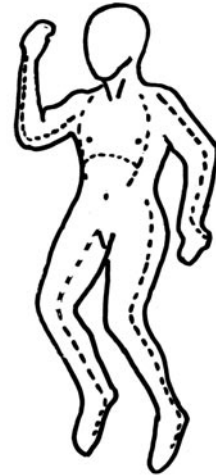
It is important to recognize that successful management of thermal injury requires a diversified and multidisciplinary approach. The goal at major burn centers is to facilitate long-term rehabilitation and functional reintegration of burn victims back into the mainstream of society. Currently, the plan of patient care starts before the patient is admitted to the burn center. As soon as the burn team is aware of the situation, a master plan is outlined. All disciplines are involved, so that a discharge plan is started which will be revised as the patient improves and progresses. "State of

the art" techniques of nursing, surgery, rehabilitation, etc., are implemented, so that the best possible outcome is obtained.

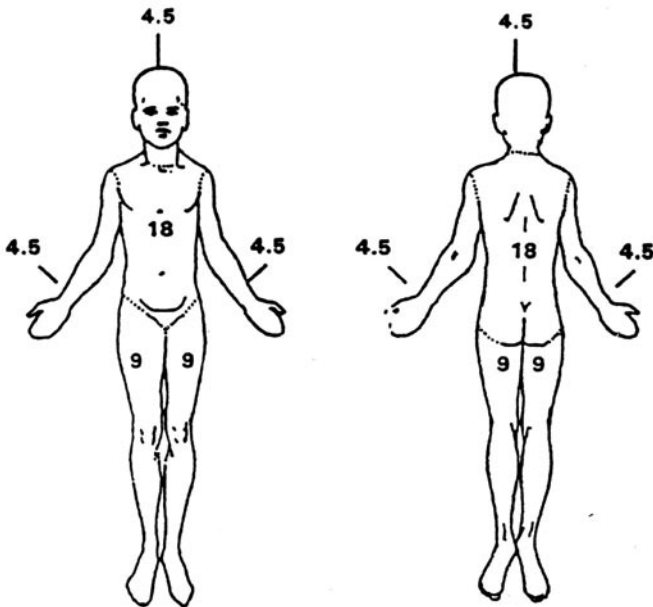
### **Initial assessment of the burn patient**

The initial physical examination of the burn victim should focus on assessing the airway, evaluating hemodynamic status; accurately determining burn size, and assessing burn wound depth. Immediate assessment of the airway is always the first priority when examining a burn patient. Massive airway edema can develop, leading to acute airway obstruction and death. If there is any question whatsoever as to the adequacy of the airway, prompt endotracheal intubation is mandated. The next step is to place two large-bore peripheral intravenous catheters since delays in resuscitation carry a high mortality<sup>25</sup>. It is also imperative during the initial assessment to make a brief survey of associated injuries. A thorough secondary survey can be postponed, but life-threatening injuries such as cardiac tamponade, pneumothorax, hemothorax, and flail chest must be identified and treated quickly. In burns over 20% TBSA, a nasogastric tube should routinely be placed to prevent gastric distension and begin early enteral feedings. A Foley catheter should be placed to monitor urine output because this is the most straight-forward and reliable indicator of intravascular volume status in the majority of these patients. Inhalation injury is currently the first cause of death in burn patients; therefore, it should be diagnosed and treated promptly. Inhalation injury can be defined most simply as a chemical tracheobronchitis that results from inhalation of the incomplete products of combustion<sup>20</sup>. The diagnosis of smoke-inhalation injury is best made based on a combination of clinical signs and thorough bronchoscopic evaluation. A history of being burned in an enclosed space, loss of consciousness, impaired mental status, associated drug or alcohol use, or concomitant head injury should alert the clinician to the possibility of an inhalation injury. Physical examination that reveals singed nasal vibrissae, facial burns, and the presence of carbonaceous sputum should raise the index of suspicion for a significant smoke-inhalation injury. Signs of wheezing, stridor, or hoarseness signal impending airway obstruction and mandate prompt intervention. Management of inhalation injury consists of ventilatory support (high frequency ventilation<sup>2</sup>, permissive hypercapnia), aggressive pulmonary toilet, bronchoscopic removal of casts, and nebulization therapy with heparin, acetylcysteine, and B2-agonists<sup>4</sup>.

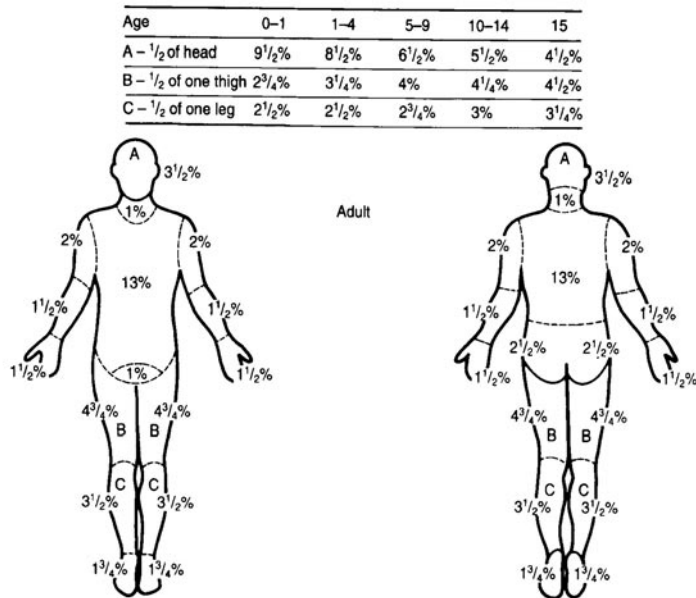
Peripheral pulses should also be assessed carefully in the acute phase. It is important to recognize that the most common early cause of diminished or absent pulses in a burn victim is inadequate resuscitation. In a circumferential burn, however, there should be a high index of suspicion for elevated subcutaneous or muscle compartment pressures. If the patient is adequately resuscitated, with normal to elevated central blood pressure and good urine output and has circumferential burns to a pulseless extremity, then an emergent escharotomy or formal fasciotomy is indicated for limb salvage. Thoracic escharotomies are also occasionally required for improving chest-wall compliance and facilitate ventilation. This is illustrated in Figure 1.



**Figure 1**  
Appropriate placement of escharotomies



**Figure 2**  
Rule of nines to determine burn size in adults

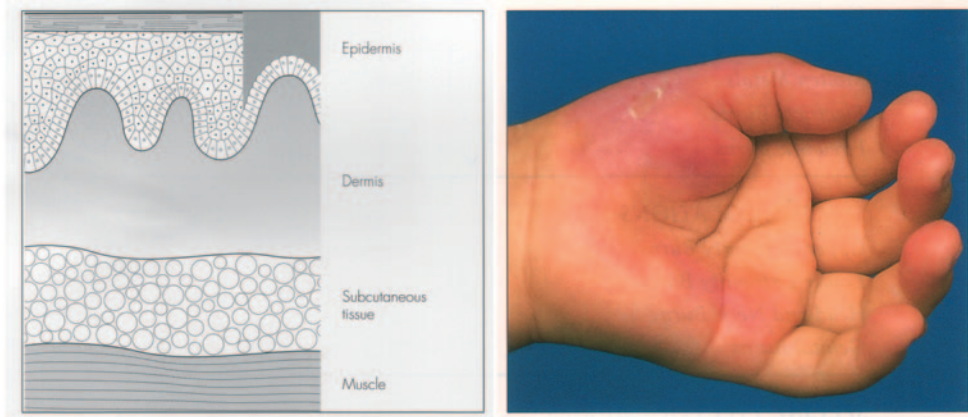
**Figure 3**

Estimation of burn size using the Lund and Browder method

### Determination of burn size and burn depth

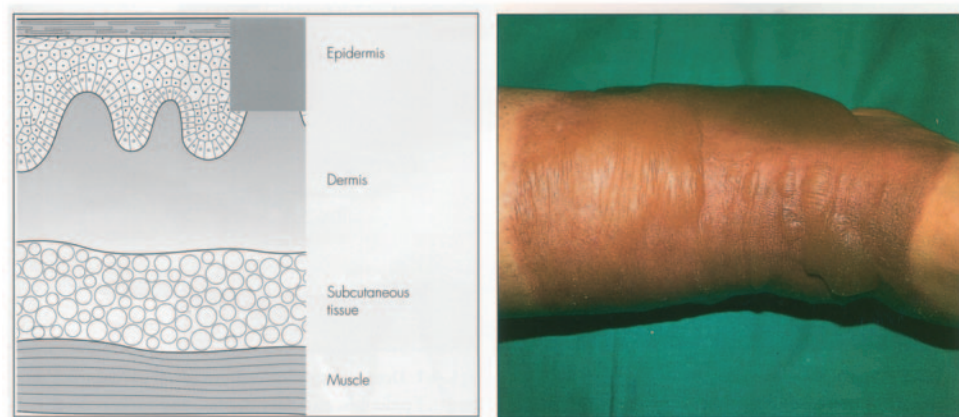
It is important to make an accurate determination of burn size, because the initial resuscitation formulas for the first 24 hours postinjury are based on the total body surface area (TBSA) burned. Several charts are available to help accurately gauge the extent of the burn injury. In adults, the rule of nines can be used to quickly estimate the size of a burn. The anterior and posterior trunk are each 18%, each of the lower extremities is 18%, each upper extremity is 9%, and the head is 9% (Figure 2). Unfortunately, the rule of nines is inaccurate in children and may overestimate burn size because the head accounts for a greater portion of the body surface area (BSA). In a 2-year-old child, this is 19% of the TBSA. Diagrams such as the Lund and Browder charts (Figure 3) are more accurate and can be used for plotting the burn size in children.

Assessing burn wound depth requires careful observation. Burns can be divided into superficial (first degree, Figure 4), partial-thickness (second degree, Figure 5), and full-thickness (third degree, Figure 6). Partial-thickness burns can be subdivided into superficial and deep partial-thickness (deep dermal) burns. There are multiple causes of thermal injury, including flame burns, scald burns, electrical injury, chemical, and contact burns. In general, first degree burns such as those from sun exposure result in sharp pain and late flaking or peeling of superficial epidermis. Second de-



**Figure 4**

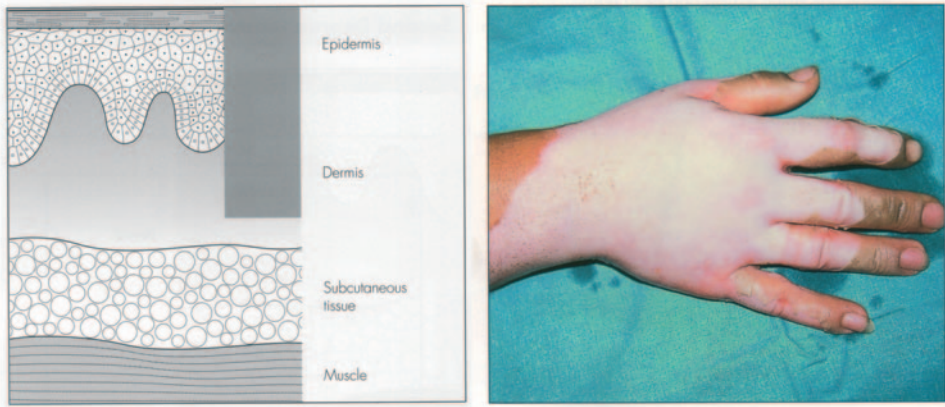
First degree burn. Only the epidermis has been damaged. Note the red, hyperemic appearance of the surface, which, along with the hyperesthesia and discomfort, is typical of these injuries.



**Figure 5a**

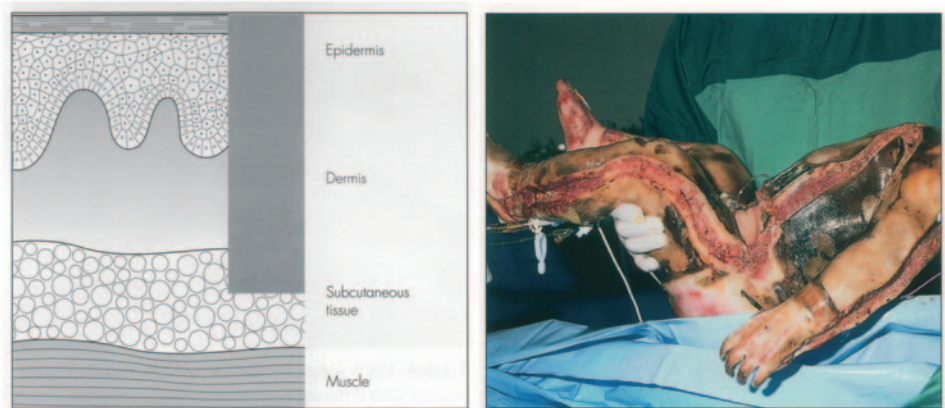
Superficial partial-thickness burn (superficial second degree). Epidermis and papillary dermis have been damaged. Blistering and extreme pain are typical of such injuries. Sensation is preserved with different degrees of hyperesthesia. Treatment is always conservative with topical antimicrobials or temporary skin substitutes.





**Figure 5b**

Deep partial-thickness burn (deep second degree). Epidermis, papillary dermis, and various depths of reticular dermis have been damaged. Note the pink-white appearance. These injuries tend to be hypoesthetic. Blistering does not normally occur, or is present many hours after the injury. A dry appearance is common. Even though these injuries can eventually heal, the optimal treatment involves excision and autografting.



**Figure 6**

Full-thickness burn (third degree). Epidermis, papillary and reticular dermis, and different depths of subcutaneous tissue have been damaged. Treatment involves excision of all injured tissue. Pain involved in these injuries is very low or absent. The potential for infection if left non-excised is very high.



gree burns are characterized by dermal involvement, excruciating pain, and the presence of blisters and serous exudate. This is in contrast to full-thickness burns, which are firm, relatively painless to light touch, and do not blanch.

### Burn Shock and Resuscitation

Hemodynamic changes after burns are significant and must be managed carefully to optimize intravascular volume, maintain end-organ perfusion, and maximize oxygen delivery to the tissues. Massive fluid shifts after severe burn injury result in the sequestration of fluid in both burned and nonburned tissue. Release of proinflammatory mediators leads to increased microvascular permeability and generalized edema. Leakage of fluid through the burn wound to the environment and into the interstitial space depletes effective circulating blood volume. Furthermore, there is also direct myocardial depression from circulating factors after burn injury<sup>16,21,23</sup>.

Many different fluid resuscitation formulas have been described, each of which

**Table 1.**  
**RESUSCITATION FORMULAS**

Evans	Normal Saline 1.0 ml/kg/% burn, Colloid 1.0 ml/kg/% burn, 2000 mL D5W
Brooke	Lactated Ringers 1.5 ml/kg/% burn, Colloid 0.5 ml/kg, 2000 ml, D5W
Parkland	Lactated Ringers 4 ml/kg/% burn, 1/2 during first 8 h postburn, the other 1/2 over next 16 h
Modified Brooke Hypertonic (Monafo)	Lactated Ringers 2 ml/kg/% burn in first 24 h 250 mEq/l Na <sup>+</sup> in volume to maintain urine output at 30 ml/h
Modified Hypertonic (Warden)	Lactated Ringers + 50 mEq Na HCO <sub>3</sub> (180 mEqNa <sup>+</sup> l for 8 h to maintain urine output at 30-50 ml/h Beginning 8 h postburn, Lactated Ringers to maintain urine output at 30-50 ml/h
Dextran (Demling)	Dextran 40 in saline at 2 ml/kg/h for 8 h Lactated Ringers-maintain urine output at 30 ml/h Fresh frozen plasma at 0.5 ml/kg/h for 18 h beginning 8 h postburn
SBH-Galveston Pediatric Formula	Lactated Ringers at 5000 ml/m <sup>2</sup> BSA burn + 2000 ml/m <sup>2</sup> BSA, 1/2 in the first 8 h postburn, the other 1/2 over the next 16 h

can be used effectively to resuscitate a severely burned patient. The various formulas differ in the amount of crystalloid and colloid to be given, as well as in the tonicity of the fluid. Table 1 illustrates the most common resuscitation formulas.

In adults, the most common formula used is the Parkland formula, which calls for the infusion of 4 ml/kg/%TBSA burn of a crystalloid solution. In the first 24 hours postburn, the initial resuscitation fluid is Lactated Ringers solution, which is isotonic to plasma. In children, maintenance requirements must be added to the resuscitation formula. For this reason, it is recommended the Shriners Burns Hospital SBH-Galveston Formula, which calls for initial resuscitation with 5000 ml/m<sup>2</sup> BSA burn/day + 2000 ml/m<sup>2</sup> BSA/day of Lactated Ringers solution. For both formulas, the first half is administered within the first 8 hours postburn, and the remaining is given over the next 16 hours. In infants, maintenance glucose must also be administered because of their low glycogen reserves to prevent critical hypoglycemia. Intravascular volume status must be reevaluated on a frequent basis during the acute phase. Closely monitoring the urine output may indicate the adequacy of resuscitation. Urine output in a child should be maintained at 1 ml/kg/h. In an adult, 0.5 ml/kg/h is sufficient. It is essential to avoid over-aggressive resuscitation, which may lead to increased extravascular hydrostatic pressure and pulmonary edema. This is especially important in patients who have a concomitant inhalation injury, because they will also have increased pulmonary vascular permeability. Administration of colloid or hypertonic solutions decreases the total amount of fluid requirements in the first 24 hours postinjury; however, no clear advantages in long-term outcomes over isotonic crystalloid resuscitations have been clinically documented.

### **Metabolic support of the burn patient**

The hypermetabolic response after burn injury is enormous and far exceeds the metabolic derangements seen in other forms of trauma. The metabolic rate may be increased as much as 2 to 3 times normal<sup>6</sup>. This response must be supported through both nutritional and pharmacologic intervention in an effort to improve net nitrogen balance, preserve lean body mass, decrease cardiac work, and diminish hepatic fatty infiltration.

Nutritional support of the hypermetabolic response is best accomplished by early enteral feeding. Total parenteral nutrition has been completely abandoned in the treatment of burns because it is associated with gut mucosal atrophy, fatty infiltration of the liver, and septic morbidity from bacterial translocation and catheter-related infection<sup>12,13</sup>. Many different formulas for calculating caloric needs in burn patients have been championed. The Curreri<sup>3</sup> formula is useful in adults and estimates caloric needs to be 25 kcal/kg/day plus 40 Kcal/%TBSA burned/day. In pediatric burns 1800 kcal / m<sup>2</sup> BSA / day plus 1300 kcal / m<sup>2</sup> TBSA burned /day is generally recommended<sup>17</sup>. In addition, electrolyte disturbances are common in burn patients and must be corrected accordingly. Finally, albumin supplementation may also be necessary during the acute phase since protein loss is extensive and hepatic synthesis of constitutive proteins is decreased as the liver accelerates its production of acute-phase proteins<sup>24</sup>.

Pharmacologic support of the hypermetabolic response is based on two major principles. The first is to use anabolic agents to preserve lean body mass and alleviate the severe muscle wasting that occurs after thermal injury<sup>19</sup>. Recombinant human growth hormone, insulin, and the combination of IGF-1 and IGF binding protein 3 (IGFBP3) have been extensively investigated with significant results<sup>7-8,22</sup>. The second is to use antiadrenergic drugs to decrease cardiac work and myocardial oxygen consumption. The most common agent currently used is propranolol, which is a nonselective B1 and B2 antagonist. In addition to decreasing heart rate and left ventricular work, propranolol administration causes decreased peripheral lipolysis, decreased tremulousness, and less irritability<sup>1</sup>.

### **Treatment of the Burn Wound**

Superficial burns normally heal within 2 weeks, and they do not need any surgical intervention. They are to be managed conservatively with twice a day washing and application of topical antimicrobial agents, such as 1% silver sulfadiazine. Applications of Biobrane (Bertek, Houston, TX) or pigskin are also options that decrease pain and facilitate healing. In contrast, full-thickness burns require formal excision and grafting. In this sort of injuries, all skin appendages have been lost, so primary healing can not be achieved. Deep partial-thickness burns are treated in a similar fashion as full-thickness burns. Formal excision and autografting is usually performed in these burns in order to achieve the best cosmetic and functional outcome. Deep partial-thickness burns have the potential to heal through regeneration from deep skin appendages. The time of complete healing, however, exceeds very often 21 days. It is now generally accepted that burn wounds that heal in more than three weeks tend to present with intense hypertrophic scarring and functional impairment. Therefore, excision and skin autografting is advocated to prevent these deformities<sup>5, 9-10,15</sup>.

### **AIM AND SCOPE OF THE THESIS**

The burn wound is the source of virtually all ill effects, local and systemic, seen in a burned patient. Surgical removal of the burn wound results in a much improved patient and, when done early, results in improvements in survival as well as in a decline of morbidity.

Burn patients were treated conservatively for many decades, allowing the burn eschar to separate by the action of human and bacterial collagenases. Patients were admitted to the most isolated wards in the hospitals, where pain, odor, and human misery were hidden. Those who survived their injuries were condemned to disfigurement and disability<sup>18</sup>.

Early excision of the burn wound gained popularity in the early 80s, when excising the entire wound within the first 2 weeks postinjury began to be feasible. The exact timing for wound excision, however, is still debatable<sup>5,11</sup>. There have been many kind of local wound treatments described, but, currently, two main approaches

are in use.

Conservative treatment of burn wounds with 1% silver sulfadiazine or cerium nitrate sulfadiazine followed by serial excision of full-thickness burns is currently the standard of care in many burn centers throughout the world. Burns are excised in areas of as much as 20% TBSA in one operative setting, and patients return to the operating room when donor sites are fully healed and ready to be harvested again. All full-thickness burns can be excised first, so that deep dermal and indeterminate depth wounds are addressed later, preventing excision of potentially viable tissue. Intraoperative and postoperative management of patients is easier, but the patient needs to return many times to the operation room, so that episodes of bacterial translocation, bacteremia, and cardiovascular instability are repeated. Other disadvantages include exaggerated blood losses, prolongation of the hypermetabolic response, and increased risk of infection and sepsis from remaining eschar in which bacteria proliferate<sup>5, 9, 15</sup>.

Immediate near-total wound excision has been advocated as an excellent alternative to serial debridement in massive burns. All full-thickness and deep partial-thickness burns are excised within 24 hours of admission, and the excised wounds are covered with autografts when feasible and homologous skin grafts or skin substitutes to other areas if the burn exceeds the donor-site supply. Infection control is easier. Burn eschars are excised completely so that burn-wound sepsis is no longer the major cause of death in these patients. Potentially viable tissue, however, may be sacrificed with this technique. It has been postulated that the surgical trauma that immediate burn-wound excision poses on patients may aggravate the inflammatory and catabolic response leading to potentially fatal complications. Furthermore, it is believed that the hemodynamic instability of burn patients during the first 72 hours after the injury makes the surgical management of burn patients more prone to postoperative complications. Therefore, many authors still question the safety and efficacy of immediate burn-wound excision in massive burns, preventing the spread of this technique<sup>10, 15</sup>.

The question remains open, however, as to when and to what extent it is best to utilize surgical wound closure in patients with burns so extensive that their survival is problematic.

### **The Pediatric Patient**

The burn injury produces overwhelming physiological and psychological challenges to a pediatric victim. The unique anatomical and physiological attributes of children make the treatment of acute pediatric trauma and burn injury much more difficult than in the general population. Furthermore, due to their anatomy and growing physiology children are more prone to complications and, if not diagnosed and treated promptly, to death. Physicians and nurses need to be trained not only in burn care, but also in the specifics of pediatric care. The provision of medical care can induce an additional trauma if developmental needs are not addressed.

The most obvious differences between adults and children are in size and body

proportions, requiring the provision of special equipment and supplies which reflect the configurations of pediatric anatomy. Due to their small body sizes, fluid losses are proportionally greater in children, making resuscitation and stabilization during burn surgery more difficult. Fluid shifts occur also very rapidly, thus continuous monitoring and titration is mandatory. The smaller aperture of the pediatric trachea predisposes it to obstruction. As edema develops, airway evaluation and management must be given priority in pediatric patients. Available stores to support prolonged starvation are critically absent in children, therefore, pediatric patients are more sensitive to the catabolic response initiated by burn injury. Furthermore, the metabolic rates of growing children are significantly higher than those predicted for adults with similar burn injuries, producing transient and permanent changes in growth patterns. Delivery of care must be tailored to the specific needs of each child in terms of their neurocognitive development and physiologic status and growing pattern.

The treatment of acute trauma in children is the most challenging and difficult enterprise of all sort of acute health management, far exceeding the complexity of adult trauma treatment. The limited physiologic reserve of children together with their hemodynamic lability makes surgical intervention extremely challenging. Given all the former particulars of the pediatric population and taking the massive pediatric burn as a paradigm of burn injury, the present thesis will focus on the pediatric burned victim.

### **Aim of the thesis**

The purpose of the present thesis is to test the hypothesis that immediate burn wound excision of massive pediatric burns is safe and efficacious, presenting with negligible postoperative complications and with salutary effects on the inflammatory and catabolic response after burn injury.

In order to evaluate immediate burn-wound excision of pediatric burns, the following questions have to be answered:

1. *What are the exact consequences of immediate burn-wound excision and massive blood transfusion in severe pediatric burns related to postoperative complications and to morbidity and mortality? (Chapter 2 and 3)*
2. *What is the impact of burn wound excision on bacterial colonization and invasion? (Chapter 4)*
3. *Are all pediatric patients candidates for immediate burn wound excision? (Chapter 5)*
4. *What are the impact and the efficacy of Cultured Epidermal Autografts in massive pediatric burns? (Chapter 6)*
5. *Does immediate burn-wound excision increase the inflammatory and catabolic response of children after burn injury? (Chapter 7)*
6. *Does conservative treatment and delayed burn-wound excision increase the inflammatory and catabolic response in children? (Chapter 7)*

7. *Can pharmacologic intervention abrogate the catabolic response of severe pediatric burns together with immediate burn-wound excision? (Chapter 8)*

The answers to these questions are addressed in the following chapters.

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